Label-free detection of biomarkers of multiple sclerosis with EGOT-based biosensors

K. Solodka[1], M. Berto[1], F. Biscarini[1,2], C.A. Bortolotti[1], M. Pinti[1]

[1]Department of Life Sciences, University of Modena and Reggio Emilia, Modena, Italy; [2]Center for Translational Neurophysiology of Speech and Communication (CTNSC), Istituto Italiano di Tecnologia, Ferrara, Italy

kateryna.solodka@unimore.it

INTRODUCTION

Multiple sclerosis (MS) is a chronic and inflammatory disorder of the central nervous system characterized by progressive neurodegeneration.[1] So far, no specific biomarker of the disease has been identified. However, in the last years, neurofilament light chain (NF-L) has emerged as a potential marker of the ongoing axonal degeneration in MS pathology. Following processes accompanied by axonal injury, this protein is released in significant amounts into the interstitial fluid, and eventually into cerebrospinal fluid (CSF) and blood, reaching abnormal levels. Therefore, CSF and blood NF-L levels could be useful to provide an indication of axonal injury, axonal loss, and neuronal death.[2]

The accurate detection and quantification of biomarkers of neural degeneration is an urgent need to correctly assess the diagnosis of MS and the management of the disease. Therefore, highly sensitive methods, able to detect very low concentrations of the biomarker and discriminate MS patients from healthy individuals are required. Here, we propose a novel electrolyte-gated organic transistor (EGOT)-based biosensor, for the detection of NF-L.

EXPERIMENTAL SECTION

The biosensors were based on electrolyte-gated organic field-effect transistors (EGOFETs). The transistors were fabricated using quartz substrates with interdigitated Au Source and Drain electrodes, spin-coated with TIPS-pentacene.

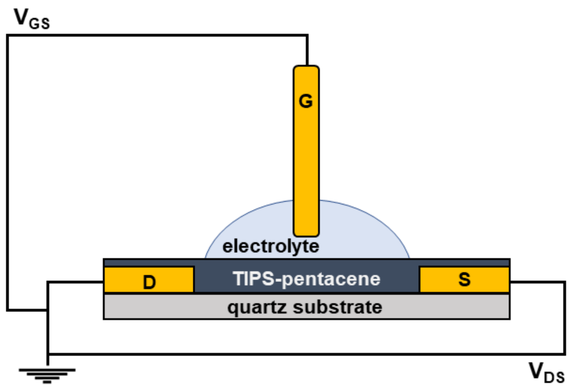

Figure 1. Schematic drawing of the experimental setup of an EGOFET device comprising the electrical connections. In order to mimic physiological conditions, all electrical measurements were carried out using PBS (50 mM, pH 7.4) as electrolyte solution.

Anti-NF-L antibodies were immobilized on the Au gate electrode with a controlled and uniform orientation by using cys-Protein G.[3]

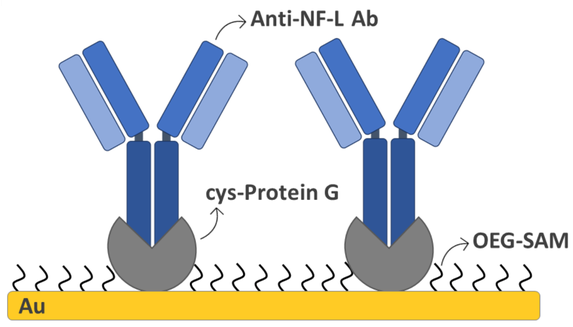

Figure 2. Schematic representation of the gate functionalization process.

RESULTS

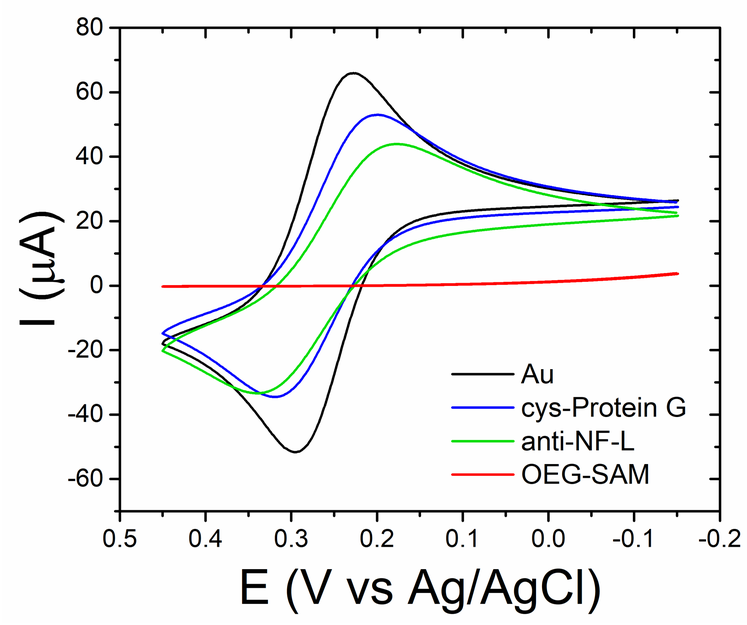

Figure 3. *E*lectrochemical characterization of every gate Au functionalization step. Cyclic voltammograms were recorded in 5 mM $K_3[Fe(CN)_6]$, 0.1 M KCl at a scan rate of 50 mV/s.

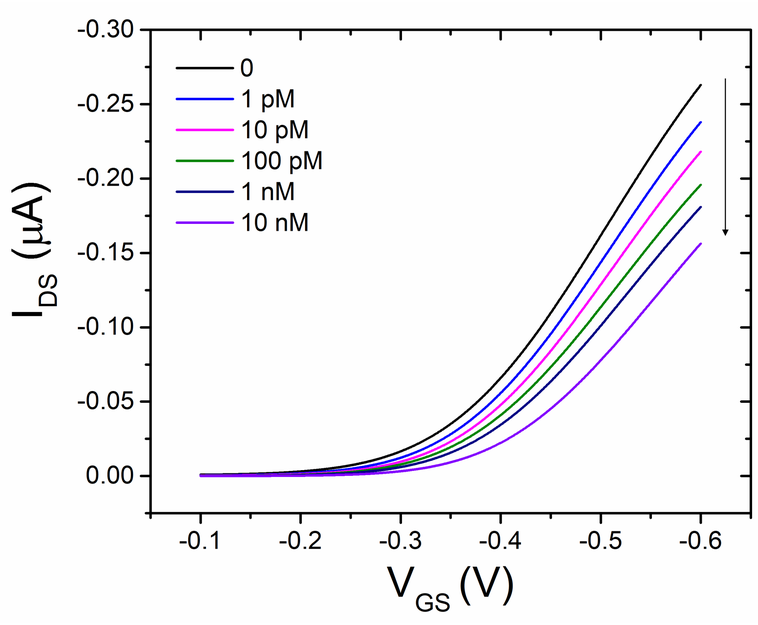

Figure 4. Transfer characteristics of an EGOFET-based biosensor upon exposure to increasing concentrations of NF-L in 50 mM PBS, ranging from 1 pM to 10 nM as reported in the legend. Transfer curves were recorded at a fixed V_{DS} of -0.2 V.

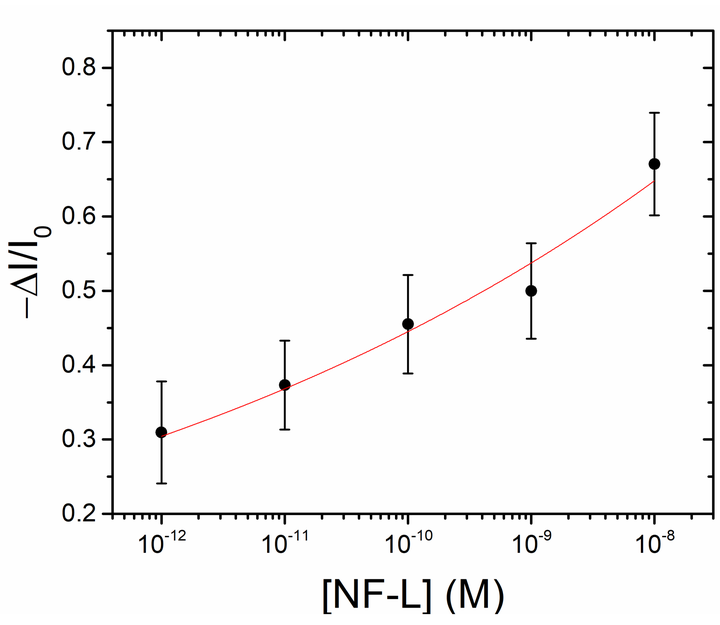

Figure 5. Biosensor dose curve $-\Delta I/I_0$ vs molar concentration of NF-L, calculated at V_{GS}=-0.4 V. Each data point is the average of n=8 independent experiments, and the error bars represent ± SE (standard error).

CONCLUSIONS AND PERSPECTIVES

In the present work, we demonstrated the successful operation of EGOFET-based biosensors for the detection of NF-L, a candidate MS biomarker. The biosensors showed high selectivity for the detection of NF-L in a wide dynamic range of concentration. Furthermore, control experiments demonstrated the absence of a non-specific response..

In order to improve the biosensor technology, further experiments will be focused on the integration of a microfluidic setup with the EGOFET architecture. Additionally, plasma samples from MS patients and controls will be analysed to evaluate the retention of selective response in highly complex media.

References

[1] A. Compston, A. Coles, *Lancet,* **2008**, *372*, 1502

[2] C. Barro, P. Benkert, G. Disanto, C. Tsagkas, M. Amann, Y. Naegelin, D. Leppert, C. Gobbi, C. Granziera, Ö. Yaldizli, Z. Michalak, J. Wuerfel, L. Kappos, K. Parmar, J. Kuhle, *Brain*, **2018**, 141, 2382-2391

[3] M. Berto, E. Vecchi, L. Baiamonte, C. Condò, M. Sensi, M. Di Lauro, M. Sola, A. De Stradis, F. Biscarini, A. Minafra, C.A. Bortolotti, *Sens. Actuators B Chem.* **2019**, 281, 150-156

Aknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the Marie Skłodowska-Curie grant agreement no. 813863.